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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/893,321
Filing Date: June 27, 2001
Appellant(s): WALKE ET AL.

Lance Ishimoto
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 6/22/04.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct. However, upon further review and in view of Appellants' arguments, all rejections under 35 USC 112, first paragraph, have been withdrawn except for the rejection under 35 USC 112, first paragraph, based on the rejection under 35 USC 101.

(7) Grouping of Claims

The rejection of claims 1-6 under 35 USC 101 and the corresponding rejection under 35 USC112, first paragraph, stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7). Appellants' statement that the rejection of claims 3 and 4 under 35 USC 112, first paragraph, as lacking written description and enablement do not stand or fall together is moot in view of the Examiner's withdrawal of these rejections.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Skolnick, J. et al "From genes to protein structure and function:novel applications of computational approaches in the genomic era." Trends in Biotech, vol 18, no. 1 (2000), pp. 34-39

Bork, P. "Powers and pitfalls in sequence analysis:the 70% hurdle." Genome Research, vol. 10 (2000), pp. 398-400.

Doerks, T, et al. "Protein annotation:detective work for function prediction." Trends in Genetics, vol 14, No. 6 (June 1998), pp. 248-250.

Smith, TF, et al. "The challenges of genome sequence annontation or "the devil is in the details." Nature Biotechnology, vol. 15 (November 1997), p. 1222-1223.

Brenner, SE. "Errors in genome annotation." Trends in Genetics, vol. 15, No. 4 (April 1999), p. 132.

Bork, P. et al. "Go hunting in sequence databases but watch out for the traps." Trends in Genetics, vol. 12, No. 10 (October 1996), pp. 425-427.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

A. Claim Rejections - 35 USC § 101

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific and substantial asserted utility, or a well-established utility. This rejection is set forth in prior Office Action mailed 3/10/03 and is reiterated in full below. These claims are directed to an isolated nucleic acid comprising at least 80 contiguous bases of SEQ ID NO:1, or 3, nucleic acid molecules which encode the protein of SEQ ID NO:2, or 4 and those which hybridize to SEQ ID NO:1, or to the complement thereof, as well as expression vectors and cells. However, the invention encompassed by these claims has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines (published 1/5/01, 66 FR 1092; M.P.E.P 2107). The instant application has provided nucleotide (SEQ ID NO:1 and 3) and protein (SEQ ID NO:2 and 4) sequences. SEQ ID NO:3 and 4 are

truncated versions of SEQ ID NO:1 and 2, respectively, so only SEQ ID NO:1 and 3 will be discussed here for simplicity. The instant application does not disclose a specific and substantial biological role of the nucleic acid molecule of SEQ ID NO:1, or the protein of SEQ ID NO:2, or their significance. Therefore, no specific and substantial utility of these nucleic acid molecules, has be asserted, nor correlation to any disease state.

It is clear from the instant specification that the claimed receptor is what is termed an "orphan receptor" in the art. Appellants disclose in the specification that the receptor encoded for by the claimed nucleic acid molecule is believed to encode a protein (termed "NHP" for "novel human protein") related to animal GABA proteins (page 1, lines 9-12). However, the basis that the receptor is disclosed in the specification to be homologous to GABA proteins is not predictive of use. There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Appellants' claimed invention is incomplete.

The instant situation is directly analogous to that of which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a

patent is not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."

The specification discloses that the polynucleotide of the invention (SEQ ID NO:1) encodes a protein which shares "sequence homology with animal GABA proteins." However, this is not a specific and substantial asserted utility, or a well established utility of the protein of the instant specification. No comparisons between the sequence of the protein of the present invention and any GABA protein has been disclosed in the specification, nor does the specification disclose that the protein encoded for by the polynucleotide of the present invention has biological activities similar to GABA proteins. Sequence homology alone is seldom sufficient in the absence of supporting evidence, because the relevant literature acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases.

For example, Skolnick et al. (Trends in Biotech. 18:34-39, 2000) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (Genome Research 10:398-400, 2000) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (Trends in Genetics 14:248-250, 1998) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (Nature Biotechnology 15:1222-1223, 1997) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. By example, PTH and PTHrP are two structurally closely related proteins which can have opposite effects on bone resorption (Pilbeam et al. Bone 14:717-720, 1993; see p. 717, second paragraph of Introduction).

Brenner (Trends in Genetics 15:132-133, 1999) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, most homologs must have different molecular and cellular functions. Finally, Bork et al. (Trends in Genetics 12:425-427, 1996) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan the utility of the claimed polynucleotide of SEQ ID NO:1, which is only known to encode a protein which shares "sequence homology with animal GABA proteins."

Therefore, the instant claims are drawn to a nucleic acid molecule which has a yet undetermined function or biological significance. There is no actual and specific significance which can be attributed to said nucleic acid molecule, or encoded protein, identified in the specification. For this reason, the instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, or any significance of the nucleic acid molecule of the present invention, which has not been disclosed in the specification as having any specific or substantial utility, there is no immediately obvious patentable use for them. To employ the nucleic acid molecule of the instant invention to treat, to better understand disease, or to use it to produce a receptor protein to identify substances which bind to and/or mediate activity of the said receptor is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for the nucleic acid molecule of the invention, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

Therefore, since the polynucleotides of SEQ ID NO:1 and 3 do not have a specific, substantial, or credible utility, or a well-established utility, then the polynucleotides comprising at least 80 contiguous bases of SEQ ID NO:1 or 3, or the claimed expression vectors and cells, also do not possess utility.

B. Claim Rejections - 35 USC § 112, first paragraph - enablement

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the claimed invention is not supported by a specific and substantial asserted utility, or a well established utility. This rejection is set forth in on page 5 of the Office Action mailed 3/10/03 and is reiterated in full below. Specifically, since the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Argument

A. Claim Rejections - 35 USC § 101

Appellants argue that "an invention is useful under section 101 if it is capable of providing some identifiable benefit" and that "any utility of the claimed compounds is sufficient to satisfy 35 USC 101." However, as stated under the current utility guidelines (published 1/5/01, 66 FR 1092), the claimed invention needs to be supported by a specific and substantial asserted utility, or a well-established utility. Appellants further argue that the presently claimed sequence is clearly referred to GABA receptor, as can be seen, for example, in the title of the invention. This argument has been considered, but is not deemed persuasive. Respectfully, though Appellants suggest that the sequence(s) of the present invention encodes GABA proteins, this is speculative. There is no data to support this assertion. It cannot be concluded that the protein of the present invention is a GABA protein simply because the specification states that it is

believed to be an ion channel on the basis of homology alone. Furthermore, there is some contradiction between, for example, the title, which recites "GABA receptors" and the specification which recites GABA subunit. Therefore, it is not clear whether Appellants believed they were in possession of a GABA subunit, or an entire GABA receptor, which consists of 5 subunits comprising three different subunit subtypes.

Appellants further cite in *In re Brana*, their major argument being that "further research does not preclude a finding that the invention has utility" and that "further research and development" is (may be) necessary. However, In re Brana, as stated by Appellants, is concerned with the utility of *pharmaceutical compositions* whereas the present invention is concerned with alleged GABA *polynucleotides*. Appellants make no mention in their arguments of Brana that the compounds, themselves, to be used in the pharmaceutical compositions do not have utility. Appellants only state that Brana is concerned with the *pharmaceutical compositions* comprising these compounds. Appellants discuss the significance of the FDA and Phase II testing regarding Brana. However, these issues are not relevant in this situation. If Appellants were claiming that the protein of the present invention, or nucleic acids encoding this protein, could be used in pharmaceutical compositions, that would be analogous. However, the proteins or polynucleotides, themselves would first need to possess utility in order for the pharmaceutical composition to possess utility. Since the proteins of the present invention do not possess utility, any comparison to Brana is, respectfully, misguided.

On pages 6-7 of the Appeal Brief dated 6/22/04, Appellants argue that it was asserted that the sequences of the present invention encode a novel mammalian ion channel protein (e.g. specification in title, on page 2, lines 4-5 and page 16, lines 7-9) that shares structural similarity with known GABA receptor proteins. Appellants further argue that the functions of GABA receptors are well-known in the art (Chapter 16 of "Basic Neurochemistry..."; also Wong et al.; Bambilla et al. and Jakobs et al.)) and that the artisan would recognize the protein of the present invention as a GABA receptor since it shares

99% amino acid identity to GenBank Q8N1C3. Again, these arguments imply that Appellants believed they were in possession of an entire GABA receptor. Even, *arguendo*, Appellants believed they were clearly in possession of a GABA subunit as opposed to the entire receptor, it appears from Appellants' arguments that they were in possession of a precursor protein, not the fully processed form and that, more importantly, Appellants did not identify this protein as a gamma subunit, let alone a gamma-1 subunit precursor, as an alignment with GenBank Q8N1C3 would suggest. Appellants argue that the fact that this protein was named a gamma-1 subunit precursor is, basically, irrelevant since this is only a name assigned to the protein at a later date. However, even allowing Appellants leeway regarding the characterization of this subunit as a gamma-1, the fact remains that Appellants did not disclose that they were in possession of a gamma subunit, regardless of whether it was considered a "1," or a "2," etc. In other words, even giving Appellants the benefit in that they were aware that the protein of their invention encoded a GABA subunit, and not an entire GABA channel protein, they still did not disclose which family of subunits their protein belonged. It is well-known in the GABA art that each subunit family, e.g. alpha, beta, gamma, have specific roles. The fact that GABA receptors as a whole are known to have a specific function is, respectfully, not relevant. The Examiner is not, as suggested by Appellants, refuting Appellants' asserted utility. The issue is the fact that Appellants have not provided any information regarding to which family of subunits their protein belongs demonstrates that Appellants have not provided a specific or substantial utility for the protein of the present invention.

Regarding the GenBank deposit, Appellants are reminded that utility has to have been present *at the time the invention was made (filed)*. Without knowing that the protein of the present invention was a gamma subunit, Appellants cannot rely on post-filing data to demonstrate this. This information could only be used if Appellants had disclosed in the specification as originally filed that they were in possession of a gamma subunit, regardless of whether or not it was a human or mouse homolog. Again, the use of CDART, as argued by Appellants, is also not persuasive since CDART analysis does not

remedy the fact that Appellants did not disclose that they were in possession of a gamma subunit. The Examiner states that, given the references cited by the Examiner in the prosecution (Skolnick et al.; Bork; Doerks et al.; Smith et al.; Brenner; and Bork et al.) a structure-function relationship among proteins is, at best, difficult. Even considering the use of bioinformatics as a potential tool to understand structure-function relationships, as argued by Appellants, Appellants have not provided the basic knowledge that the protein was a gamma subunit. Therefore, no function could be assigned to this subunit without further characterization. Again, respectfully, a patent is not a hunting license. The fact that the protein of the invention may have ultimately been identified as a gamma subunit does not remedy the fact that this information was not known at the time of filing.

Appellants argue that many U.S. Patents using bioinformatics have issued. As stated by Appellants and as agreed upon by the Examiner, all U.S. Patents are presumed valid. Appellants also argue that, according to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. 101 as allegedly lacking a patentable utility and under 35 U.S.C. 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence (such as the presently claimed sequence) that has a similarity score of 95% to a protein having a known function. In the Analysis portion of Example 10 it states that "Based on applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO:2 encodes a DNA ligase. Further DNA ligases have a well-established use in the molecular biology art based on this class of proteins ability to ligate DNA."

This argument has been considered, but is not deemed persuasive. First, unlike the Training Example, the claims of the present invention do not provide a function. It is clear that the sole function of a DNA ligase is to ligate DNA. Therefore, the artisan would know the specific function of a newly

identified DNA ligase. However, the artisan would not know the specific function of a novel GABA channel subunit without knowing to which family it belongs.

Appellants argue that the present invention can be used as a specific marker of the gene encoding the GABA receptor (subunit) of the present invention and that the polynucleotide can be used with 'gene chip' technology, on which entire industries are based. They further argue that only a small number of nucleic acid molecules can be used to track gene expression since only a small number (2-4%) of nucleotide sequences are expressed. They further argue that expression profiling does not require a knowledge of the function of the particular nucleic acid on the gene chip. These arguments have been considered, but are not deemed persuasive. The use of the polynucleotide of the present invention in such applications as the Human Genome Project does not confer a specific use for the polynucleotide of the present invention, or its encoded protein. In other words, though the Human Genome Project itself may be substantial and credible, it does not provide a substantial or specific utility of the polynucleotide of the present invention. Similarly, the argument that the claimed polynucleotide sequences can be used to track the expression of the genes encoding the described proteins, or that uses such as "for DNA chips," "chromosomal mapping," or other "markers" is not persuasive since these uses, again, are neither specific or substantial since any nucleotide sequence can be used in such an assay. While it is clear that the nucleic acid molecule of the present invention would hybridize to a chromosome, without knowing the function of the protein encoded for by this nucleic acid molecule, then simply identifying that a nucleic acid molecule localizes to a particular region of a chromosome would not provide a use for the nucleic acid molecule of the present invention. In contrast to Appellants' argument, the Examiner is not stating that the GABA receptor subunit of the present invention has to have a unique utility, as the function of GABA receptors as a whole is generally known. The core issue, again, is that Appellants have not identified the protein of the invention as a gamma subunit, regardless of whether or not this utility is "unique."

B. Claim Rejections - 35 USC § 112, first paragraph - enablement

A. Appellants argue that the claimed invention is enabled because it has utility as argued previously. Appellants' arguments have been fully considered, but are not found to be persuasive for the reasons discussed above under 35 USC 101.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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July 6, 2004

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